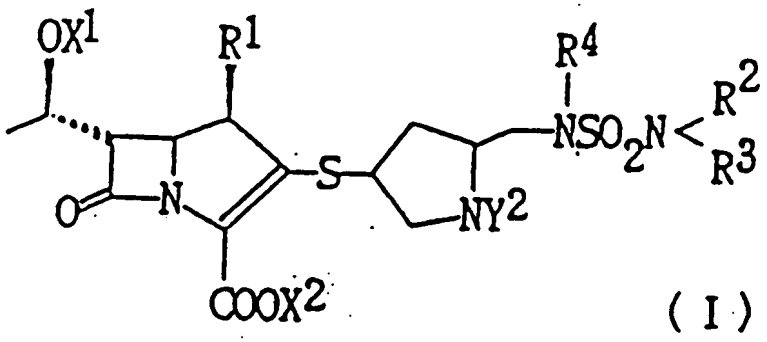
Claims 12-17 have been withdrawn from consideration by the Examiner as being drawn to nonelected inventions.

The Invention

The pyrrolidylthiocarbapenem derivative of this invention is represented by Formula I:



(I)

wherein R^1 is hydrogen or lower alkyl; R^2, R^3 and R^4 are hydrogen, lower alkyl which can be substituted or an amino protecting group independently, or R^2 and R^3 together with a nitrogen atom to which R^2 and R^3 are bonded to form a saturated or unsaturated cyclic group, or R^2 and R^4, or R^3 and R^4 together with two nitrogen atoms and one sulfur atom in the sulfamide group to form a saturated or unsaturated cyclic group; each cyclic group can further include at least on atom selected from the group consisting of oxygen, sulfur and nitrogen, and each cyclic group can be substituted; X^1 is hydrogen or a hydroxy protecting group; X^2 is hydrogen, a carboxy protecting group, an ammonio group, an alkali metal or an alkaline-earth metal; and Y^2 is hydrogen or an amino protecting group.

Rejection of Claims 1-11 and 18-22 under 35 U.S.C. 103

Claims 1-11 and 18-22 are rejected under 35 U.S.C. 103 as being unpatentable over Murata U.S. Patent No. 4,963,543. (Murata '543)

The Federal Circuit has established that obviousness is determined by whether the prior art suggested to one of ordinary skill in the art that the modification of the prior art to arrive at

the invention should be carried out and would have a reasonable likelihood of success when viewed in light of the prior art.

The Examiner states that the main difference between what is claimed in the present invention and Murata '543 is in the variable attached to the "pyrrolinyl" moiety. The Examiner maintains that the motivation to prepare the claimed sulfamide (-N-SO_2-N-) type derivatives comes from the teaching in Murata that ureido (-N-CO-N-) type pyrrolinyl derivatives are all equally operative for the same purpose.

Murata '543 teaches a pyrrolinyl derivative with a ureido moiety whereas the claimed invention teaches a pyrrolinyl derivative with a sulfamide moiety. This difference in structure causes differences in the properties of the compound. First, the sulfamide moiety is acidic and can act as a dibasic acid. In contrast the ureido moiety is basic in nature. Moreover, the compounds of the present invention have increased solubility in water and therefore are available for anti-bacterial injection therapy. Further, these compounds decompose slower in the body than prior art compounds resulting in the anti-microbial effect lasting longer. Also, they are less toxic to the body. See page 25, lines 24-31 of the specification. Consequently, the sulfamide type pyrrolinyl compounds of the present invention have a stronger acidity than the ureido type pyrrolinyl compounds of Murata '543. One skilled in the art would not be motivated by Murata's disclosure of basic pyrrolinyl derivatives to produce pyrrolinyl derivatives which are acidic.

Furthermore, Applicant respectfully asserts that the ureido type systems of Murata '543 are not all equally operative for the same purpose as maintained by the Examiner. Murata '543 states at column 8, lines 5-6 and 25-26 that 2-ureidoxethyl, 1,-1-dimethyl-2-ureidoxethyl, and ureido carbonyl methyl are the "more preferable" ureido moieties.

The Examiner cites In re Lohr for his assertion that evidence of obviousness is supplied when the compounds are prepared in the same manner and possess the same utility. This case is distinguishable from the present situation. In Lohr, the difference between the prior art structure and the claimed structure was the substitution of two methyl groups at the 2 and 6 position of the hetocyclic nucleus. In Lohr there is no meaningful change in structure and properties from the prior art compound to the invention. Just a simple substitution of alkyl groups on a heterocyclic ring. This is in contrast to the present situation where the pyrrolinyl

sulfamide moiety in the present invention is different in structure and properties from the pyrrolinyl ureido type compounds of Murata '543. More importantly, the compounds of the present invention are not prepared the same as in Murata '543. See the procedures on pages 16-19, 26-80 and 84-91 of the specification. Also, they exhibit increased antibacterial utility. See the specification at page 25, lines 7-24.

Therefore, Applicant respectfully maintains that there was no motivation for one skilled in the art to take the basic ureido systems of Murata '543 and prepare the acidic sulfamide systems of the present invention. The reference relied on teaches that certain ureido systems are better than others and thus not equally operable for the same purpose. Additionally, even if one skilled in the art was motivated by Murata '543, there is no reasonable expectation in light of the prior art that an acidic pyrrolinyl sulfamide derivative of the compounds at issue could be prepared that would result in a successful antibacterial compound.

The Examiner also cites In re Payne to support the proposition that a disclosure of "ureido" type systems which are all equally operative for the same purpose supplies the necessary motivation in a prima facie case of obviousness. Payne like Lohr involved only a difference in the substituents on the heterocyclic ring of the compound as the only modification between the prior art and the claimed compounds. Moreover, as detailed previously, in the present case the modification is much more substantial. The present invention adds a sulfamide derivative which results in a compound which is more acidic, has increased solubility in water and is more stable in the body than prior art compounds. The reasoning of Payne does not apply here because of the greater change in structure and properties from the prior art.

Accordingly, Murata '543 neither suggests nor teaches compounds containing the pyrrolindine sulfamide derivatives as in the claimed compounds. Applicant asserts that the rejection under 35 U.S.C. 103 is improper and respectfully requests that the rejection of claims 1-11 and 18-22 be withdrawn with subsequent notice of allowance.

In the event the Examiner finds that minor issues of this case remain unresolved, the Examiner is respectfully requested to contact the undersigned attorney to arrange for a telephone interview to expedite the allowance of this application. In the event any fees are due in connection with the filing of this document, the Commissioner is authorized to charge those fees to our deposit account number 18-0988.

Respectfully submitted,

RENNER, OTTO, BOISSELLE & SKLAR

By _____
Neil A. DuChez
Reg. No. 26,725

1621 Euclid Avenue
Nineteenth Floor
Cleveland, Ohio 44115
(216)621-1113